

Amendment and Response After Final Rejection  
Serial No.: 09/248,964  
Attorney Docket No.: HAR-005 (6615/8)  
Page 3

toward the C-terminus, a flexible molecular linker, and a second coiled-coil dimerization;

wherein an Fc domain is covalently attached to the C-terminus of at least one of the first or second dimerization domains;

wherein the first dimerization domain and said second dimerization domain associate in solution at physiological conditions; and

an MHC binding peptide covalently bound to the at least one MHC Class II fusion protein.

132. (Amended) The MHC Class II-peptide Complex of claim 131 wherein the MHC binding peptide is covalently attached to the N-terminus of the first polypeptide chain and the Fc domain is covalently attached to the C-terminus of the second polypeptide chain.

133. (Amended) The MHC Class II-peptide Complex of claim 131 wherein the MHC binding peptide is covalently attached to the N-terminus of the second polypeptide chain and the Fc domain is covalently attached to the C-terminus of the first polypeptide chain.

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#### REMARKS

Claims 1-20, 103, and 114-133 are pending, and claims 1-20 are withdrawn from consideration. Claims 103, 114, 115, 122, 125, and 131-133 are amended herein, and Applicants do not intend to disclaim equivalents thereof. Applicants respectfully request entry of these amendments as they do not raise new issues of patentability, respond to the Office Action, and place the claims in condition for allowance. Accordingly, Applicants request reconsideration and withdrawal of the rejections and allowance of the claims as provided herein. To the extent the claims 103 and 114-133 are found allowable, Applicants will act on withdrawn claims 1-20.

#### Drawing

Applicants submit a courtesy copy of a Transmittal of Substitute Formal Drawing and a substitute formal drawing (sheet 10 of 10) in compliance with the May 7, 2002, Draftsperson's Review.

Amendment and Response After Final Rejection  
Serial No.: 09/248,964  
Attorney Docket No.: HAR-005 (6615/8)  
Page 4

Rejections under 35 U.S.C. § 112, First paragraph

Claims 125-128 and 131-133 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 125-127 were rejected for allegedly lacking support for the recitation of an MHC Class II fusion protein further comprising a first immunoglobulin Fc domain positioned at the C-terminus of one of the first and second polypeptide chains. Support for this recitation is found in the specification, for example, at page 12, lines 15-19, at page 23, line 16 to page 24, line 28, and in Figure 2. Accordingly, Applicants respectfully traverse this rejection.

Claim 128 was rejected for allegedly lacking support for the recitation of an MHC Class II fusion protein further comprising a first flexible molecular linker covalently linking the MHC Class II  $\alpha$  chain to the first dimerization domain and a second flexible molecular linker covalently linking the MHC Class II  $\beta$  chain to the second dimerization domain. Support for this recitation is found in the specification, for example, at page 5, lines 20-22, at page 12, lines 15-19, page 23, at line 16 to page 24, line 28, and in Figure 2. Accordingly, Applicants respectfully traverse this rejection.

Claims 131-133 were rejected for allegedly lacking support for the recitation of an MHC Class II fusion protein where an Fc domain is covalently attached to the C-terminus of one of the first and second dimerization domains. Support for this recitation is found in the specification, for example, at page 12, lines 15-19, at page 23, line 16 to page 24, line 28, and in Figure 2. Accordingly, Applicants respectfully traverse this rejection.

Rejections under 35 U.S.C. § 112, Second paragraph

Claims 114, 125-127, and 131-133 were rejected under 35 U.S.C. § 112, second paragraph. Claim 114 is amended herein to add the word "residues." Claim 125 is amended herein to recite "at least one of the first or second polypeptide chains." Claim 131 is amended herein to recite "at least one of the first or second dimerization domains." Claim 131 also is amended herein to recite "the at least one MHC Class II fusion protein." Claims 132 and 133 are

Amendment and Response After Final Rejection  
Serial No.: 09/248,964  
Attorney Docket No.: HAR-005 (6615/8)  
Page 5

amended herein to depend from claim 131. Accordingly, Applicants respectfully submit that the rejections have been overcome and request withdrawal of these rejections.

Rejections under 35 U.S.C. § 102(a)/103(a)

Claims 103, 122-123, and 129 were rejected under 35 U.S.C. § 102(a) over Scott *et al.* (May, 1996), *J. Exp. Med.*, 183:2087-2095 ("Scott") and U.S. Patent No. 5,837,816 to Ciardelli *et al.* ("Ciardelli"). Claims 114-115 and 118-119 were rejected under 35 U.S.C. § 102(a) over Scott and Kalandadze *et al.* (August 16, 1996), *J. Biol. Chem.*, 271(33):20156-20162 ("Kalandadze"). Claims 116-117 and 120-121 were rejected under 35 U.S.C. § 103(a) over Scott. Claim 124 was rejected under 35 U.S.C. § 103(a) over Scott in view of Ciardelli. Claim 130 was rejected under 35 U.S.C. § 103(a) over Scott in view of U.S. Patent No. 6,015,884 to Schneck *et al.* ("Schneck"). Applicants do not acquiesce to these rejections. However, in order to advance prosecution of this patent application to allowance, Applicants amend independent claims 103 and 131 herein to recite, in part, an extracellular domain of a human MHC Class II  $\alpha$  chain and an extracellular domain of a human MHC Class II  $\beta$  chain. Support is found in the specification, for example, at page 27, line 28 to page 28, line 2. Additionally, Applicants note that Kalandadze does not appear to qualify as prior art and will not be commented upon further.

Scott reports on the engineering of a soluble murine MHC class II molecule, IA, whose pairing has been forced by the addition of leucine zipper peptide dimers at their COOH-terminus. Ciardelli reports on a method of preparing a soluble, hetero-oligomeric mammalian polypeptide by culturing a host cell transformed or transfected with an expression vector encoding a fusion protein comprising a leucine zipper domain and a heterologous mammalian peptide such as the ectodomains of IL-2 receptors. Schneck reports on soluble recombinant divalent and multivalent analogs of heterodimeric proteins which link a polypeptide chain of a heterodimeric transmembrane protein to an immunoglobulin heavy chain and a second polypeptide chain of a heterodimeric transmembrane protein to an immunoglobulin light chain.

Scott is the basis of all of the rejections under 35 U.S.C. §§ 102(a) and 103(a). Scott, either alone or in combination with the other references, does not teach or suggest the inventions recited in amended independent claims 103 and 131 having an extracellular human MHC Class

Amendment and Response After Final Rejection  
Serial No.: 09/248,964  
Attorney Docket No.: HAR-005 (6615/8)  
Page 6

II  $\alpha$  chain and an extracellular domain of a human MHC Class II  $\beta$  chain. Furthermore, one skilled in the art would not have been motivated to modify Scott with the requisite reasonable expectation of success to obtain the inventions recited in amended independent claims 103 and 131. On page 2088, left column, Scott states "We have successfully expressed a number of soluble and secreted HLA-DR molecules in SC2 insect cell but had failed to produce large quantities of the murine IA molecules by using the same approach." Further, in the sentence carrying over from page 2088 to page 2089, Scott states "Promiscuous chain pairing by IA and HLA-DQ has been demonstrated by the existence of mixed isotype molecules on B cell lines. The ability of IA molecules to form mixed isotype dimers suggests a low  $\alpha$ - $\beta$  pairing efficiency." Thus, Scott itself teaches that one approach which is successful in producing soluble and secreted HLA-DR molecules is not successful for murine IA molecules. As such, Applicants believe that one skilled in the art would understand that murine and human MHC Class II proteins are different when it comes to their assembly into molecules according to the invention, for example, based upon their pairing properties. That being the case, Applicants believe that one skilled in the art would not have the requisite expectation of success in applying the teaching of Scott to an extracellular domain of a human MHC Class II  $\alpha$  chain and an extracellular domain of a human MHC Class II  $\beta$  chain in order to obtain the inventions recited in amended independent claims 103 and 131.

It is respectfully submitted, for the reasons provided above, that amended independent claims 103 and 131 are both novel and non-obvious, and claims 114-129, 132, and 133, which depend either directly or indirectly from allowable base claims, also are allowable. Accordingly, Applicants respectfully submit that these rejections are overcome and request that these rejections be withdrawn.

Amendment and Response After Final Rejection  
Serial No.: 09/248,964  
Attorney Docket No.: HAR-005 (6615/8)  
Page 7

On the basis of the foregoing amendments and remarks, Applicants submit that claims 103 and 114-133 are in condition for allowance and requests early and favorable action.

Respectfully submitted,



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Amendment and Response After Final Rejection  
Serial No.: 09/248,964  
Attorney Docket No.: HAR-005 (6615/8)  
Page 8

Marked-up Version of Amended Claims for U.S.S.N. 09/248,964

103. (Twice Amended) A Class II Major Histocompatibility Complex fusion protein comprising

a heterodimer of a first polypeptide chain and a second polypeptide chain;

wherein the first polypeptide chain comprises a fusion of, toward the N-terminus, an extracellular domain of a[n] human MHC Class II  $\alpha$  chain and, toward the C-terminus, a first coiled-coil dimerization domain;

wherein the second polypeptide chain comprises a fusion of, toward the N-terminus, an extracellular domain of a[n] human MHC Class II  $\beta$  chain and, toward the C-terminus, a second coiled-coil dimerization domain; and

wherein the first dimerization domain and said second dimerization domain associate in solution at physiological conditions to form a heterodimer capable of selectively binding an MHC binding peptide.

114. (Amended) The MHC Class II fusion protein of claim 103 wherein the extracellular domain of the MHC Class II  $\alpha$  chain comprises residues 5-180 of an MHC Class II  $\alpha$  chain.

115. (Amended) The MHC Class II fusion protein of claim 103 wherein the extracellular domain of the MHC Class II  $\alpha$  chain comprises residues 5-200 of an MHC Class II  $\alpha$  chain.

122. (Amended) The MHC Class II fusion protein of claim 103 wherein at least one of the dimerization domains comprises a leucine zipper domain.

125. (Amended) The MHC Class II fusion protein of claim 103 further comprising a first immunoglobulin Fc domain positioned at the C-terminus of at least one of the first [and] or second polypeptide chains.

131. (Amended) A MHC Class II-peptide complex comprising  
at least one Class II MHC fusion protein comprising

Amendment and Response After Final Rejection  
Serial No.: 09/248,964  
Attorney Docket No.: HAR-005 (6615/8)  
Page 9

a heterodimer of a first polypeptide chain and a second polypeptide chain;  
wherein the first polypeptide chain comprises a fusion of, toward the N-terminus, an extracellular domain of a[n] human MHC Class II  $\alpha$  chain and, toward the C-terminus, a flexible molecular linker, and a first coiled-coil dimerization domain;

wherein the second polypeptide chain comprises a fusion of, toward the N-terminus, an extracellular domain of a[n] human MHC Class II  $\beta$  chain and, toward the C-terminus, a flexible molecular linker, and a second coiled-coil dimerization;

wherein an Fc domain is covalently attached to the C-terminus of at least one of the first [and] or second dimerization domains;

wherein the first dimerization domain and said second dimerization domain associate in solution at physiological conditions; and

an MHC binding peptide covalently bound to the at least one MHC Class II fusion protein.

132. (Amended) The MHC Class II-peptide Complex of claim [132] 131 wherein the MHC binding peptide is covalently attached to the N-terminus of the first polypeptide chain and the Fc domain is covalently attached to the C-terminus of the second polypeptide chain.

133. (Amended) The MHC Class II-peptide Complex of claim [132 claim 132] 131 wherein the MHC binding peptide is covalently attached to the N-terminus of the second polypeptide chain and the Fc domain is covalently attached to the C-terminus of the first polypeptide chain.